EXHIBIT I

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BOEHRINGER INGELHEIM INTERNATIONAL GMBH and BOEHRINGER INGELHEIM PHARMACEUTICALS, INC., Plaintiffs,	)	C.A. No. 05-700 (***)
v.	)	
BARR LABORATORIES, INC. Defendant.	)	

EXPERT REPORT OF RICHARD B. MAILMAN, Ph.D.

I. Background and Qualifications

1. I hold an appointment as tenured Professor in the Departments of Psychiatry, Pharmacology, and Neurology in the School of Medicine, and in the Division of Medicinal Chemistry and Natural Products in the School of Pharmacy at the University of North Carolina at Chapel Hill.

2. I received a Ph.D. in Physiology with a minor in Toxicology in 1974 from North Carolina State University ("NCSU"), and received subsequent post-doctoral training from both NCSU and the University of North Carolina in toxicology, neuropharmacology, and neuroscience. I have been working in the field of neuropharmacology, neurotoxicology, and neuroscience for over 30 years.

3. I have published more than 200 peer-reviewed research papers, chapters, and reviews, as well as two books. I have had funding for my research from the National Institutes of Health for nearly 30 years.

4. I regularly teach courses in pharmacology, including to medical students, medical residents and fellows, and graduate students, as well as to students in the Pharmacy Doctorate

program. I also participate in higher-level teaching in neuroscience and drug discovery and development. In addition, I consult with physicians from time-to-time regarding the use of centrally-acting drugs.

5. I have held positions such as Director of the Division of Basic Psychobiology in the Department of Psychiatry, and Associate Director of the Curriculum in Toxicology, and currently serve in several administrative positions.

6. I have trained more than two dozen Ph.D.s and more than a dozen post-doctoral fellows in the fields of pharmacology, neuroscience, toxicology, and medicinal chemistry, and have mentored numerous young faculty members. Individuals that I have trained or mentored now include the Dean of a Big Ten Medical School, three Departmental Associate Chairs, as well as scientists having senior positions with several pharmaceutical companies.

7. I have extensive experience in the discovery and early development of pharmaceuticals, including drug discovery and early preclinical drug development. I also have participated in later drug developmental activities including the design of human trials. One of the primary thrusts of my research has been drugs for dopamine receptors, the targets for drugs like Mirapex®. I have particular expertise in a class of drugs known as dopamine agonists, and how these drugs work in several central nervous system disorders including Parkinson's disease and schizophrenia. I have led a research program that provided new approaches for the treatment of Parkinson's disease.

8. I am a Fellow of the American College of Neuropsychopharmacology, and a member of the American Society for Pharmacology and Experimental Therapeutics, the American Chemical Society, the Society for Neuroscience, the American Society of Neurochemistry, the International Society for Neurochemistry, the American Association for the

Advancement of Science, and the Society of Toxicology. I have served on several national committees for some of these professional societies.

9. I have won several scientific awards including the Burroughs-Wellcome Scholar in Toxicology Award from the Society of Toxicology.

10. Over the past 20 years, I have served as a consultant to several pharmaceutical companies regarding drug discovery and development issues.

11. I have served or am currently serving on the editorial boards of many journals including Current Opinion in Central and Peripheral Nervous System (CPNS) Drugs, the Journal of Molecular and Biochemical Toxicology, Neurotoxicology, Synapse, Neurochemistry International, Neurotoxicology and Teratology (Neurochemistry Field Editor), Fundamental and Applied Toxicology, Brain Research Bulletin, Psychopharmacology Bulletin (Associate Editor), and the Journal of Molecular Neurobiology. In addition, I am a regular reviewer for scientific and medical journals. For example, in the last twelve months I have reviewed manuscripts for the Journal of Pharmacology and Experimental Therapeutics, Molecular Pharmacology, the American Journal of Psychiatry, Neuropsychopharmacology, Neuroscience Letters, Brain Research, European Journal of Pharmacology, Expert Opinion in Investigational Drugs, Expert Opinion in Pharmacotherapy, FASEB Journal, Journal of Neurochemistry, Journal of Medicinal Chemistry, and Psychopharmacology, among others.

12. During the last four years, I have testified as an expert in the following case:

- *Eli Lilly Canada, Inc. v. Novopharm, Ltd.* (Canadian Federal Court File No. T-1532-05)

13. I am being compensated for my time at the rate of $500 per hour. My compensation is in no way dependent on the outcome of this case.

14. My curriculum vitae are attached as Exhibit A.

II. Mandate

15. I have been asked to comment on and respond to issues raised by Dr. C. Warren Olanow's report, as well as to address issues related to experiments disclosed in the Eli Lilly U.S. Application Serial No. 747,748. In that regard, I will testify as an expert in the fields of neuroscience and neuropharmacology, including drug discovery and development and mechanisms of action of drugs in the central nervous system.

16. In addition to the specific opinions set forth in this report, I may respond to additional testimony and information that becomes available during deposition, at trial, or otherwise, including any opinions put forth by Boehringer's experts. I also may use charts, graphs, or other demonstrative exhibits to support any potential testimony at trial, as well as provide further background information on principles of neuroscience and neuropharmacology, including drug discovery and development and mechanisms of action of drugs in the central nervous system.

17. In forming my opinions, I have relied on the materials cited throughout this report and listed in Exhibit B, as well as my training and experience.

III. Definition of One of Ordinary Skill in the Art

18. With respect to the issues I address in this report, a person of ordinary skill in the art as of the priority date[1] (the "skilled artisan") would have a Ph.D. in pharmacology, physiology, toxicology, or neuroscience, and/or an M.D. degree with post-graduate training in neurology, or equivalent training or experience. In addition, the skilled artisan would have some

[1] I have been asked to assume that the relevant priority date is December 22, 1984, but my opinions would not change if December 19, 1985 were used as the priority date instead.

familiarity with, or an understanding of, the drug discovery and development process as it relates to neuroscience and/or neuropharmacology.[2]

IV. Dr. Olanow's Report

A. Mirapex® and Pramipexole

19. Throughout his report, Dr. Olanow refers to pramipexole and Mirapex® interchangeably—a convention I adopt in this report as well—and associates the properties of the compound pramipexole, which is a free base, with the administration of Mirapex®, which contains pramipexole in the form of a dihydrochloride salt. That association is reflective of the skilled artisan's understanding, both as of the priority date and today, that the use of pramipexole to treat various conditions will involve the use and formation of both the free base and protonated forms of the compounds.

20. The skilled artisan would understand, both as of the priority date and today, that regardless of whether one administers pramipexole as a method of treating a condition—for example, treating parkinsonism or Parkinson's disease, treating schizophrenia, lowering blood pressure, or lowering heart rate—or administers the acid addition salt of pramipexole as a method of treating that condition, a natural result of practicing those methods will be the formation of pramipexole in both protonated (both mono- and diprotonated) and unprotonated (free base) forms. The skilled artisan would possess this understanding based on the principle

[2] In my view, Dr. Olanow's definition of the person of ordinary skill in the art as "physicians and scientists" is too broad and does not accurately reflect the level of ordinary skill in the art. However, to the extent the training and experience of the skilled artisan is determined to be broader than the definition described in my report—for example, to also encompass scientists and physicians with substantial experience in the research or treatment of central nervous system disorders such as Parkinson's disease, restless leg syndrome, fibromyalgia, or depression—it would not change my opinions.

that weak acids and bases will be in dynamic equilibrium in biological systems and hence will be present in both protonated and unprotonated forms. That principle is reflected in the Henderson-Hasselbalch equation and analogous equations for diprotic acids, which can be used to calculate how much of a compound such as pramipexole will be protonated and how much will exist as pramipexole itself (a free base) at different pH levels. Indeed, the skilled artisan would possess the same understanding about the compounds used in at least claims 8, 9, 18, 19, 28, 29, 38, and 39 of the U.S. Patent No. 4,843,086 ("the '086 patent")—*i.e.*, that whether those compounds are administered in free base or acid addition salt form to treat a condition, a natural result of practicing those methods will be the formation of the compounds in both protonated (both mono- and diprotonated) and free base forms.

21. Dr. Olanow's discussion is limited to the (S)-enantiomer of 2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole.[3] He does not discuss any properties of (R)-2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole (or an acid salt thereof) or any mixture of these two enantiomers, including the racemic mixture. I am not aware of any evidence demonstrating that (R)-2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole, or any acid salt thereof: (1) satisfied any long-felt need in the medical community; or (2) possesses any of the therapeutic properties discussed by Dr. Olanow.

B. Restless Leg Syndrome

22. To the extent that Dr. Olanow suggests that, as of the priority date, the skilled artisan would not expect that pramipexole could be used in the treatment of restless leg syndrome (also called "restless legs syndrome"), I disagree.

[3] Ex. 51; BARR 209410-12 (Merck Index, 14th edition, p. 7707).

23. The skilled artisan would understand from claims of the '086 patent that pramipexole was a dopamine agonist. He would possess that understanding based on, among other things, the claimed methods of use and the structure of the compounds used in those methods.

24. As of the priority date, it was known that dopamine agonists, the class of compounds to which pramipexole belongs, could be used in the treatment of restless leg syndrome. In a 1982 Letter to the Editor in the Archives of Neurology—a peer-reviewed publication of the American Medical Association and one of the journals cited and relied upon by Dr. Olanow—Dr. Akpinar described a study that had been conducted in multiple patients involving the use of dopaminergic therapy to treat the symptoms of "moderate to severe" restless leg syndrome.[4] The letter reported the following: (1) a dopaminergic therapy (*i.e.*, administration of the Parkinson's combination therapy of levodopa plus the decarboxylase inhibitor benserizide) caused "complete disappearance of restless leg symptoms"; (2) administration of bromocriptine mesylate (a dopamine agonist) "gave similar good results"; and (3) a dopamine antagonist "worsened the symptoms." Based on these results, a person of ordinary skill in the art as of the priority date would agree with the conclusion stated in the article that "levodopa plus benserazide (or a dopamine agonist) can be used successfully in the treatment of restless leg syndrome."

25. Dr. Olanow comments on whether pramipexole satisfied any "longstanding unmet medical need" with respect to the treatment of restless leg syndrome. Olanow ¶ 39(b). I note that ropinirole was approved by FDA for the treatment of moderate-to-severe primary restless

[4] Akpinar, S. (1982) Treatment of Restless Legs Syndrome With Levodopa Plus Benserazide. *Arch. Neurol.* **39**:739.

leg syndrome before pramipexole. To my knowledge, pramipexole has not been shown to have a particular advantage over ropinirole in treating RLS. To the contrary, one of the references authored and relied on by Dr. Olanow indicates that 32% of RLS patients treated with pramipexole developed augmentation, but that no augmentation was reported with ropinirole.[5]

C. Neuroprotection

26. Dr. Olanow states that a neuroprotective therapy is considered to be the most important unmet medical need in PD, and adds that "[n]o currently available therapy has as yet been established to have neuroprotective effects in PD." Olanow ¶ 28. I agree. However, to the extent Dr. Olanow suggests that pramipexole is neuroprotective in Parkinson's disease—either in slowing or stopping (1) disease progression, or (2) the development of non-dopaminergic features—or that it has satisfied the medical need for neuroprotective therapy, I disagree.

27. The evidence does not support the conclusion that pramipexole can actually be used as a neuroprotective agent. Dr. Olanow concludes that pramipexole is neuroprotective based the following: (1) pramipexole has been shown to protect dopamine neurons from a variety of toxins in laboratory models, and (2) a clinical double-blind trial showed that patients treated with pramipexole had a slower rate of decline of a biomarker of Parkinson's disease—specifically, a marker of the number of surviving nigrostriatal dopamine neurons. Olanow ¶ 29.

28. With regard to the first point, Dr. Olanow errs in assuming that "protection" in animal and *in vitro* models equates to clinical neuroprotection. Unfortunately, such neuroprotection models have generally not had a high degree of success in predicting clinical

[5] Tse W, Koller W, and Olanow CW. *Restless legs syndrome: differential diagnosis and treatment*, in Chaudhuri KR, Odin P, and Olanow CW, eds, *Restless Legs Syndrome*, Taylor & Francis (London) 2004.

effects. As an example, in a paper cited by Dr. Olanow regarding a laboratory study,[6] levodopa is one of the "toxins" used to show the "protective" action of pramipexole. Yet the recent ELLDOPA clinical study conducted by the Parkinson's Study Group has shown that levodopa does not hasten the progression of Parkinson's signs and symptoms as would be expected from such a "toxin."[7] Indeed, these clinical data suggest that levodopa actually may be somewhat neuroprotective.[8]

29. With regard to Dr. Olanow's second point, he states that a clinical double-blind trial[9] demonstrated that pramipexole-treated patients "had a slower rate of decline of a biomarker of nigrostriatal dopamine neurons . . . [and that those] . . . findings are consistent with the possibility that pramipexole may be neuroprotective in PD." Olanow ¶ 29. However, the biomarker used in the cited study is a radioligand that labels the dopamine transporter. It is known in the literature that the level of measurable dopamine transporters can change when

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[6] Zou L, Jankovic J, Rowe, DB, Xie, W, Appel S, and Le W (1999) Neuroprotection By Pramipexole Against Dopamine- And Levodopa-Inducted Cytotoxicity. *Life Sci.* **64:**1275-1285.

[7] Stanley Fahn and the Parkinson Study Group (2005) Does levodopa slow or hasten the rate of progression of Parkinson's disease? *J. Neurol.* **252** (Suppl 4):IV/37-IV/42; Chan PL, Nutt JG, and Holford NH (2007) Levodopa Slows Progression of Parkinson's Disease. External Validation by Clinical Trial Simulation. *Pharm. Res.* **24**:791-802.

[8] This is not a unique example of the lack of the clinical predictability of such laboratory models as commonly used. Coenzyme Q_{10} has been suggested by such models to be neuroprotective, but recent clinical studies showed no such effect. Beal MF, Matthews RT, Tieleman A, and Shults CW (1998) Coenzyme Q_{10} attenuates the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced loss of striatal dopamine and dopaminergic axons in aged mice. *Brain Res.* **783**:109-114; Storch A, Jost WH, Vieregge P, Spiegel J, Greulich W, Durner J, Müller T, Kupsch A, Henningsen H, Oertel WH, Fuchs G, Kuhn W, Niklowitz P, Koch R, Herting B, and Reichmann H (2007) Randomized, Double-blind, Placebo-Controlled Trial on Symptomatic Effects of Coenzyme Q_{10} in Parkinson Disease. *Arch. Neurol.* **64**:E1-E6.

[9] Parkinson Study Group (2002) Dopamine Transporter Brain Imaging to Assess the Effects of Pramipexole vs Levodopa on Parkinson Disease Progression. *JAMA*, **287**:1653-61.

drugs that bind to D_2 receptors (such as pramipexole) are administered.[10] In other words, because the marker used to assess neuroprotection can be affected by pramipexole in ways that are unrelated to neuroprotection, the clinical study relied on by Dr. Olanow does not demonstrate that pramipexole is in fact neuroprotective.

30. In paragraph 30 of his report, Dr. Olanow states that the "notion that pramipexole would be neuroprotective in the treatment of PD was not known to persons of ordinary skill in the art (physicians and scientists) at the time of the original invention." While the evidence does not support the conclusion that pramipexole is neuroprotective in the treatment of PD, practicing any claim of the '086 patent which encompasses a method of using pramipexole to treat parkinsonism or Parkinson's disease would necessarily result in the use of pramipexole as a neuroprotective agent if the compound indeed had such properties.

D. Fibromyalgia

31. To the extent that Dr. Olanow suggests pramipexole can be used to treat fibromyalgia, or that it satisfied any unmet need in the treatment of fibromyalgia, I disagree. Current evidence does not demonstrate that pramipexole is an effective treatment for fibromyalgia.

32. Dr. Olanow asserts that physicians occasionally prescribe Mirapex® to treat fibromyalgia, and suggests those prescriptions are indicative of whether the drug can be used to treat fibromyalgia. Olanow ¶ 44. However, because the precise cause of fibromyalgia is unclear,[11] an array of medications is often tried in the hope that one might work. Moreover, the

[10] Williams JM and Galli A (2006) The Dopamine Transporter: A Vigilant Border Control for Psychostimulant Action. *Handb. Exp. Pharmacol.* **175**:215-32.

Holman article[12]—the only published study cited by Dr. Olanow to support his opinion that Mirapex® treats fibromyalgia—is flawed. As an example, the biggest improvement was noted when the pramipexole was stopped in the last week of the trial. It also was an add-on study that provides no evidence that pramipexole by itself would work as well as commonly-used therapies for fibromyalgia (such as NSAIDs or antidepressants), or indeed, work at all. Finally, recent literature confirms that, despite the availability of Mirapex®, researchers are still searching for an appropriate means of treating fibromyalgia.[13]

E. Depression

33. Dr. Olanow states that the "notion that pramipexole would be effective in the treatment of depression was not known to persons of ordinary skill in the art (physicians and scientists) at the time of the original invention," Olanow ¶ 48, and adds that "[n]o other anti-parkinsonian drug has been shown to have anti-depressant effects," Olanow ¶ 46. I disagree. The skilled artisan would have known as of the priority date that bromocriptine, a dopamine agonist and anti-parkinsonian drug, had been shown to have antidepressant effects.[14] Moreover, as of the priority date, the skilled artisan would have known that bromocriptine had been shown

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[11] Abeles AM, Pillinger MH, Solitar BM, and Abeles M (2007) Narrative Review: The Pathophysiology of Fibromyalgia. *Ann. Intern. Med.* **146**:726-734.

[12] Holman AJ and Myers RR (2005) A Randomized, Double-Blind, Placebo-Controlled Trial of Pramipexole, a Dopamine Agonist, in Patients With Fibromyalgia Receiving Concomitant Medications. *Arthritis & Rheum.* **52**:2495-2505.

[13] Clayton AH and West SG (2006) Combination Therapy in Fibromyalgia. *Curr. Pharm. Design.* **12**:11-16.

[14] Bouras N and Bridges PK (1982) Bromocriptine in depression. *Curr. Med. Res. Opin.* **8**:150-153; Theohar C, Fischer-Cornelssen K, Brosch H, Fischer EK, and Petrovic D (1982) A Comparative, Multicenter Trial between Bromocriptine and Amitriptyline in the Treatment of Endogenous Depression. *Arzneimittelforschung.* **32**:783-787.

to have antidepressant effects in patients with Parkinson's disease.[15] Therefore, as of the priority date, the skilled artisan would not regard any anti-depressant activity of pramipexole to be unexpected.

34. To the extent pramipexole has anti-depressant effects in patients with Parkinson's disease, practicing any claim of the '086 patent which encompasses a method of using pramipexole to treat parkinsonism or Parkinson's disease would necessarily result in the treatment of PD depression if pramipexole indeed has such a property.

V. Eli Lilly

35. Tables 1 and 2 of the Eli Lilly '748 Application show that the compound being used in those experiments inhibited prolactin secretion and caused turning in the rat model. Indeed, in the mid-1980s, a skilled artisan would select these particular tests to evaluate the dopamine agonist activity of a given compound. In addition, Table 3 shows that the compound being used in that experiment caused blood pressure and heart rate decreases. Further, Table 4 shows that the compound being evaluated decreased heart rate and blood pressure.

36. In the 1980s, and even today, a compound that was expected to possess dopamine agonist activity would also be expected to be useful in connection with the treatment of parkinsonism or Parkinson's disease.

July 9, 2007

Date

Richard B. Mailman, Ph.D.

[15] Jouvent R, Abensour P, Bonnet AM, Widlocher D, Agid Y, and Lhermitte F (1983) Antiparkinsonian and Antidepressant Effects of High Doses of Bromocriptine. An Independent Comparison. *J. Affect. Disord.* 5:141-145.

EXHIBIT A

CURRICULUM VITAE
RICHARD BERNARD MAILMAN

PERSONAL INFORMATION:

Address:	7001C NC Neurosciences Hospital (Express) [CB#7160 (US Mail)] University of North Carolina School of Medicine Chapel Hill, N.C 27599-7160	
Home Address:	2101 N. Lakeshore Dr. Chapel Hill, N.C 27514	Web: http://www.med.unc.edu/wrkunits/2depts/pharm/faculty/mailman.htm
Contact Information:	919.966.2484 *Office* 919.933.8909 *Home*	919.966.9604 *Fax* richard_mailman@med.unc.edu *Email*
Citizenship:	U.S.	Research Interests: Receptor signaling and molecular drug design; novel therapeutics for Parkinson's disease, cognition, and schizophrenia

EDUCATION:

B.S.	1968	Rutgers University	Chemistry/Food Science
M.S.	1972	North Carolina State University	Physiology/Toxicology
Ph.D.	1974	North Carolina State University	Physiology/Toxicology
Post-doctoral	1974-75	North Carolina State University	Drug metabolism
Post-doctoral	1976-77	Univ. of North Carolina, Chapel Hill	Neurobiology

EMPLOYMENT HISTORY:

(All Positions at the University of North Carolina School of Medicine)

1988-present:	Professor, Departments of Psychiatry, Pharmacology, Neurology, and Medicinal Chemistry Director, Division of Basic Psychobiology (since 1994) Director, Post-doctoral Training, Curriculum in Toxicology (since 2007) Member, Neurobiology and Toxicology Faculties (since 1978)
1987-1988:	Associate Professor (tenured), Psychiatry and Pharmacology
1980-1987:	Research Associate Professor, Psychiatry and Pharmacology
1978-1980:	Research Assistant Professor, Psychiatry

HONORS AND AWARDS:

Burroughs Wellcome Fund Scholar in Toxicology (1987-1992)

Distinguished Neuroscience Professor, Purdue University, September 2003

1999 Eugene Hargraves Award in Mental Health Research

First Distinguished Alumni Keynote Speaker, Department of Toxicology, North Carolina State University, 1998.

Burroughs Wellcome Fund Research Travel Award (1999-2000)

Early admissions, Rutgers University; New Jersey State Scholarship; Rutgers College Dean of Men's Grant

American Society of Biological Chemists-Brand Travel Grant, 1974

PROFESSIONAL SOCIETIES:

American College of Neuropsychopharmacology *(Member 1984; Fellow, 1989; Finance Committee 1987-92; Liaison Committee with Government Agencies and the Pharmaceutical Industry; 1994-1997)*

Society for Neuroscience; American Society of Neurochemistry; International Society for Neurochemistry; American Society for Pharmacology and Experimental Therapeutics; American Chemical Society; American Association for the Advancement Science;

Society of Toxicology *(Program committee, 1988-92; Ethics Committee 1987-92; Councilor, Neurotoxicology Section, 1981)*

PROFESSIONAL SERVICES

APPOINTMENTS TO U.S. FEDERAL REVIEW COMMITTEES:

NIH ZRG1 MDCN-L (2001-present); Session Chair, NIMH Consensus Panel (MATRICS) on Neuropsychopharmacological Treatment of Cognition (2003); NIH Toxicology Study Section (1987-1991); NIMH Special Projects Reviews (1984-1987) NIH Reviewers Reserve (1991-1995); NIMH Neuroscience of Mental Health Workshop (1993); EPA Science Review Panel for Health Research (1984-1989); Numerous NIH ad hoc reviews every year since 1990.

EDITORIAL BOARD ACTIVITY:

Current Opinion in Central and Peripheral Nervous System (CPNS) Drugs (1998-present)
The Journal of Molecular and Biochemical Toxicology (1993-present)
Neurotoxicology (1986-1999)
Synapse (1993-2004)
Neurochemistry International (1981-1988)
Neurotoxicology and Teratology (Neurochemistry Field Editor, 1985-1989)
Fundamental and Applied Toxicology (1989-1995)
Brain Research Bulletin (1989-1995)
Psychopharmacology Bulletin (Associate Editor, 1988-1997)
The Journal of Molecular Neurobiology (1988-2000)

Regular Reviewer for many scientific and medical journals. In 2006, I reviewed papers for:
American Journal of Psychiatry
Biochemical Pharmacology
Brain Research
Current Pharmacogenomics
Environmental Health Persepctives
European Journal of Medicial Chemistry
European Journal of Pharmacology
Expert Opinion in Pharmacotherapy
Journal of Medicinal Chemistry
Journal of Neurochemistry
Journal of Pharmacology and Experimental Therapeutics
Molecular Pharmacology
Neuropsychopharmacology
Psychopharmacology

FEDERAL RESEARCH FUNDING

NIH MH073910 (W.C. Goddard III, PI; R.Mailman, Subcontract PI). Title: Subtype specific agonist for D1-D5 dopamine receptors. Funding Period: 01/01/06-12/31/07.

PREVIOUS FEDERAL GRANT SUPPORT (AS PI):

NIH R01 MH 40537. Title: A Novel Molecular Site for Antidopaminergic Action
P.I.: RB Mailman; Funding Period: 4/1/85-1/31/

NIH R01 NS39036. Title: Molecular Regulation of D_1 Dopamine Receptor Function
P.I.: RB Mailman; Funding Period: 9/30/00-08/31/06

NIH R01 MH53356 (P.I. 1997-2002)
NIH PO1 ES01104 (Program Director 1986-1992; Project P.I. from 1980-1992);
NIH RO1 ES05279 (P.I.: 1990-1994);
NIH RO1 MH37404 (P.I.: 1984-9);
NIH RO1 HD13487 (P.I. 1980-4);
NIH R23 ES02087 (P.I.: 1978-81);
EPA CR809644 (P.I.: 1981-5).

PUBLICATIONS

Summary: 2 books, 6 patents, 200+ peer-reviewed research papers and chapters (Supplementary list of > 200 book reviews, editorial comments, and published abstracts available upon request)

BOOKS:

1. Hodgson, E, RB Mailman and JE Chambers. Macmillan Dictionary of Toxicology. Macmillan Scientific, London. 395 pp., 1988.
2. Hodgson, E, RB Mailman and JE Chambers. Macmillan Dictionary of Toxicology (Second Edition). Macmillan Scientific, London. 608 pp., 1998.

PATENTS:

1. Nichols, DE and Mailman RB US 5,420,134. "Substituted hexahydrobenzo[*a*]phenanthridines" (05/30/1995) (plus foreign patents)
2. Nichols, DE and Mailman RB US 5,959,110: "Fused isoquinolines as dopamine receptor ligands"(09/25/99) (plus foreign patents).
3. Nichols, DE and Mailman RB US 6,194,423: "Fused isoquinolines as dopamine receptor ligands"(02/27/01) (plus foreign patents).
4. Nichols, DE and Mailman RB. US 6,413,977 "Chromeno[4,3,2-DE]isoquinolines as potent dopamine receptor ligands" (07/03/2002) (plus foreign patents).
5. Mailman, RB, Huang, X, and Nichols DE. US 6,916,823 "Method of treatment of dopamine-related dysfunction" (07/12/2005) (plus foreign patents)
6. Nichols, DE and Mailman RB. US 6,916,832 "Chromeno[4,3,2-DE]isoquinolines as potent dopamine receptor ligands" (07/12/2005) (plus foreign patents).

REFEREED ARTICLES (CHRONOLOGICAL ORDER):

1. Mailman, RB, E Hodgson and D Huisingh. Effect of thiols in reversing the inhibition by methyl-1-(butylcarbamoyl)-2-benzimidazolecarbamate on Saccharomyces cerevesiae. Pest. Biochem. Physiol. 1: 401-408, 1971.

2. Baker, RC, LB Coons, RB Mailman and E Hodgson. Induction of hepatic mixed function oxidases by the insecticide, mirex. Environ. Res. 5: 418-424, 1972.

3. Mailman, RB and E Hodgson. The cytochrome P-450 substrate optical difference spectra of pesticides with mouse hepatic microsomes. Bull. Environ. Contam. Toxicol. 8: 186-192, 1972.

4. Hodgson, E, RM Philpot, RC Baker and RB Mailman. Effect of synergists on drug metabolism. Drug. Metab. Dispos. 1: 391-401, 1973.

5. Kulkarni, AP, RB Mailman, RC Baker and E Hodgson. Cytochrome P-450 difference spectra. Type II interactions in insecticide-resistant and -susceptible houseflies. Drug. Metab. Dispos. 2: 309-320, 1974.

6. Mailman, RB, AP Kulkarni, RC Baker and E Hodgson. Cytochrome P-450 difference spectra: effect of chemical structure on type II spectra in mouse hepatic microsomes. Drug. Metab. Dispos. 2: 301-308, 1974.

7. Kulkarni, AP, RB Mailman and E Hodgson. Cytochrome P-450 optical difference spectra of insecticides. A comparative study. J. Agric. Food. Chem. 23: 177-183, 1975.

8. Mailman, RB, LG Tate, KE Muse, LB Coons and E Hodgson. The occurrence of multiple forms of cytochrome P-450 in hepatic microsomes from untreated rats and mice. Chem. Biol. Interact. 10: 215-228, 1975.

9. Mailman, RB, W Edmundson, K Muse and E Hodgson. Multiplicity of hepatic cytochrome P-450 in intact microsomes: effect of 3-methylcholanthrene induction. Gen. Pharmacol. 8: 281-284, 1977.

10. Mailman, RB, GT Barthalmus, K Muse and E Hodgson. Multiplicity of hepatic cytochrome P-450 in intact microsomes: effect of phenobarbital induction. Gen. Pharmacol. 8: 275-279, 1977.

11. Breese, GR, RA Vogel, CM Kuhn, RB Mailman, RA Mueller and SM Schanberg. Behavioral and prolactin responses to 5-hydroxytryptophan in rats treated during development with 5,7-dihydroxytryptamine. Brain. Res. 155: 263-275, 1978.

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BOOK CHAPTERS AND PROCEEDINGS (CHRONOLOGICAL ORDER):

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56. Mailman RB. and Huang X. Chapter 4. Dopamine Receptor Pharmacology In: Handbook of Clinical Neurology (3rd Series) Parkinson's Disease and Related Disorders (W. Koller, E. Melamed, Eds.) (in press, 2007).

57. Mailman RB. Chapter 19. Toxicant-Receptor Interactions: Fundamental Principles. Introduction to Biochemical and Molecular Toxicology, Fourth Edition, E. Hodgson and R. Smart (eds). (in press 2007)

INVITED PRESENTATIONS:

1. April, 1974. University of Cincinnati, Department of Environmental Health, Cincinnati, OH. "Multiplicity of cytochrome P450 in uninduced rats and mice."

2. September, 1974. University of Michigan, Department of Environmental and Industrial Health, Ann Arbor, MI. "Multiplicity of cytochrome P450: Effects of inducing agents."

3. August, 1978. Groningen University, Groningen, the Netherlands. Department of Medicinal Chemistry. "Is there a direct role of dopaminergic neurons in regulating cerebellar cGMP?"

4. March, 1979. University of North Carolina School of Medicine, Department of Psychiatry Grand Rounds, Chapel Hill, NC. "Lithium interactions with chronic haloperidol treatment."

5. September, 1981. Duke University, Neurobehavioral and Psychopharmacology Training Program, Durham, NC. "Drug Metabolism and Antipsychotic drugs."

6. January, 1982. National Institutes of Health - Consensus Development Symposium on "Diet and Childhood Hyperactivity", Washington, DC. "The example of red dye number 3: neurotoxin or no toxin."

7. May, 1982. National Institute of Environmental Health Sciences, Laboratory of Neurobehavioral Toxicology and Teratology, Research Triangle Park, "CNS sensitivity changes: Drugs, toxicants and receptors."

8. May, 1982. University of Minnesota, Department of Pharmacology, Minneapolis, MN. "Actions of thioridazine in vitro. Drug metabolism as an essential component of CNS action.

9. October, 1982. American Association of Cereal Chemists National Meeting, San Antonio, TX, "Sensitivity to food additives" in Symposium on "Food Allergies"

10. October, 1982. University of Texas Medical Branch, Department of Pharmacology, Galveston, TX. "Regulation of the sensitivity of dopamine neurons: Is receptor regulation the primary mechanism"

11. June, 1983. Synthelabo, Inc., Paris, France. "Are receptors always involved in supersensitivity"

12. June, 1983. Groningen University, Groningen, the Netherlands. Department of Biological Psychiatry. "Artifacts of the neuroleptic radioreceptor assay."

13. June, 1983. Groningen University, Groningen, The Netherlands. Department of Medicinal Chemistry. "Metabolism and the actions of thioridazine."

14. June, 1983. University of Uppsala and Ulleracker Hospital, Uppsala, Sweden. "Pharmacology of thioridazine."

15. August, 1983. San Diego, CA. Symposium on Molecular and Cellular Mechanisms of Neurotoxicity. "Effects of Neurotoxicants on Neurotransmitter Function".

16. March, 1984. University of Texas Medical Branch, Galveston, TX. Department of Pharmacology. "Redefining function of dopamine receptors".

17. April, 1984. Bowman-Gray School of Medicine of Wake Forest University, Winston-Salem, NC. Department of Pharmacology. "Redefining function of multiple dopamine receptors."

18. May, 1984. Northwestern University, Chicago, IL. Departments of Pathology, Physiology and Pharmacology-Minisymposium on Biochemical Mechanisms of Neurotoxicity. "Effects of Environmental Agents on Neurotransmitter Systems".

19. June, 1984. US Army Medical Research Division, Edgewood Arsenal, MD. "Redefining function of multiple dopamine receptors."

20. June, 1984. Venice, Italy, Workshop on Novel and Atypical Antipsychotic Drugs. "D_1 actions of D_2 dopamine receptor blockers".

21. October, 1984. University of Medicine and Dentistry of New Jersey-SOM, Camden, NJ. "The biochemistry of dopamine receptors and antipsychotic drugs".

22. February, 1985. University of North Carolina, Department of Medicinal Chemistry. "Benzazepines as novel probes of dopamine receptors".

23. March, 1985. University of Medicine and Dentistry of New Jersey-SOM, Camden, NJ. "Effects of low doses of lead on the central nervous system".

24. April, 1985. University of Arkansas Medical Center, Department of Pharmacology. "Multiplicity of dopamine receptors."

25. April, 1985. Medical College of Pennsylvania, Department of Pharmacology. "Multiplicity of dopamine receptors."

26. September, 1985. FASEB Symposium on Predicting Neurotoxicity and Behavioral Dysfunction from Preclinical Data. "Mechanisms of CNS Injury in Behavioral Dysfunction."

27. November, 1985. University of Pennsylvania, Department of Pharmacology. "Some aspects of the multiplicity and function of dopamine receptors".

28. December, 1985. American College of Neuropsychopharmacology - Symposium on D_1 dopamine receptors. "Multiplicity of D_1 dopamine receptors".

29. April, 1986. U.S.-Sweden Collaborative Workshop in Toxicology. National Institutes of Environmental Health Sciences, Research Triangle Park, NC.

30. August, 1986. American Chemical Society. Middle Atlantic Section, Baltimore, Md. Symposium: Chemical Indices of Neurotoxicity. "Neurotoxicants and central catecholamine systems".

31. October, 1987. Duke University Medical Center, Durham, NC. Department of Pharmacology. "D_1 Dopamine Receptors".

32. March, 1988. Purdue University. Department of Pharmacology and Toxicology. "The Pharmacology and Toxicology of D_1 Dopamine Receptors".

33. April, 1988. Health Effects Institute Annual Meeting, Colorado Springs. "Understanding the Factors Required to Detect or Predict Neurotoxicity".

34. September 7, 1988. Duke University Medical Center, Durham, NC. Interdisciplinary Program in Toxicology. Visiting Scholar. "Effect of toxic insult of dopamine receptors"

35. September 16, 1988. Burroughs Wellcome Inc., Research Triangle Park, NC. "Effect of toxic insult of dopamine receptors"

36. March 2, 1989: "Toxicant-induced biochemical and molecular changes that affect cell-cell communication". Invited talk in Symposium on "Neurotoxicant-induced alterations in cellular interactions". Society of Toxicology Annual Meeting, Atlanta, GA.

37. September 19, 1989. Advisory Council, National Institutes of Environmental Health Sciences. "Modern Approaches to Problems of Central Nervous System Toxicology".

38. September 20, 1989. Rutgers University. Department of Pharmacology and Toxicology. "Response of Dopamine Receptor Systems to Insult".

39. February 1, 1990. Yale University. Department of Pharmacology. "Are there multiple D_1 Dopamine receptors?"

40. April 25, 1990. Carrier Foundation and Clinic, Belle Mead, NJ. "Evaluating therapeutic diets: how therapeutic are they?"

41. May 19, 1990. Michigan State University. Neuroscience Program. "D_1 Dopamine receptors"

42. September 20, 1990. University of Rochester. Molecular and Biochemical Toxicology Program. "Mechanisms of Dopamine Receptor Supersensitivity"

43. February 27, 1991. Society of Toxicology Annual Meeting, Dallas TX. "New Investigators Forum".

44. April 17, 1991. N.C. Society of Toxicology Annual Meeting, Research Triangle Park, NC. "Implications of receptor mediated processes for human risk assessment: Neurotoxicants acting at receptors"

45. August 22, 1991. U.S. Environmental Protection Agency Research Center, Research Triangle Park, NC. Neurotoxicology Division. "Response to Insult of Dopamine Systems"

46. February 26, 1992. Society of Toxicology Annual Meeting, Seattle WA. Burroughs-Wellcome Award Address. "Responses of the Brain to Toxic Insult: Molecules, Models, and Medicine"

47. February 28, 1992. Oregon Health Sciences University, Vollum Institute. "New directions in function and structure of D_1 dopamine receptors"

48. April 24, 1992. FASEB Meeting. "Biochemical and molecular receptor mechanisms in synaptic responses to neurotoxic insult" in ASPET Symposium entitled: "Role of receptors and their regulatory effectors in neurotoxicity."

49. February 23, 1993. University of Florida Health Sciences Center, Gainesville. Psychiatry Grand Rounds. "Drugs for Dopamine Systems: New Directions in the Treatment of Psychiatric and Neurologic Disorders."

50. March 3, 1993. University of North Carolina, Curriculum in Toxicology. "Accommodating for Insult to Dopamine Neurons: Chemical and Idiopathic Parkinsonism."

51. February 11, 1994. Hoechst Roussel Pharmaceuticals, Bridgewater, NJ. "Molecular drug design and dopamine receptors."

52. April 15, 1994: Otsuka Pharmaceutical Corp., Osaka Japan. "Molecular Pharmacology of OPC-14597".

53. April 15, 1994: Otsuka Pharmaceutical Corp., Osaka Japan. "New Concepts of Drug Selectivity: Functional Selectivity Based on Cellular Localization".

54. October 11, 1994: Department of Toxicology, North Carolina State University. "Parkinson's Disease: Toxicological Cause? Toxicological Cure?"

55. December 8, 1994: Neurobiology Curriculum, University of North Carolina, Chapel Hill. "The Functional Selectivity Hypothesis: A Novel Mechanism Explaining Receptor-Mediated Drug Selectivity?"

56. May 17, 1995. Neurology Grand Rounds, University of North Carolina, Chapel Hill. "Molecular Drug Design and Novel Therapeutic Approaches to Treatment of Parkinson's Disease"

57. May 17-19, 1996. Antalya, Turkey. Congress: Dopamine Receptor Subtypes: From Basic Science to Clinic "Functional Effects of Novel Dopamine Ligands: Dihydrexidine and Parkinson's Disease as a First Step."

58. September 8, 1997: Department of Medicinal Chemistry, University of North Carolina, Chapel Hill. "D_1 dopamine receptors: from molecular modeling to medicine."

59. September 9, 1997: Department of Pharmacology, University of North Carolina, Chapel Hill. "D_1 Dopamine Receptors: From Computer to Clinic."

60. Oct. 9-13, 1997: Noram International Symposium on Gene and Transplant Therapy for Parkinson's Disease and Other Neurological Disorders, Beijing, China. "Advances in the Pharmacotherapy of Parkinson's Disease".

61. December 17-18, 1997: Ada County (Idaho) Medical Education Consortium "Therapy of Parkinson's Disease: Present and Future."

62. March 19, 1998. Psychiatry Grand Rounds, University of North Carolina, Chapel Hill. "Novel mechanisms for pharmacotherapy of schizophrenia and movement disorders".

63. March 21, 1998: North Carolina State University. First Annual Distinguished Alumni Lecture "Novel Therapies: An Interdisciplinary Approach".

64. November 18, 1998. Northwestern University. "Molecular design of dopaminergic ligands: novel mechanisms for pharmacotherapy of schizophrenia and Parkinson's disease".

65. 1999-01-07. University of North Carolina. Center for Alcohol Studies. "Novel receptor mechanisms influencing pharmacotherapeutic approaches to treatment of drug abuse".

66. 1999-04-15. Purdue University. Department of Medicinal Chemistry and Molecular Pharmacology "Functional selectivity: a novel mechanism of drug-receptor interaction."

67. 1999-04-16. Lilly Pharmaceuticals Inc., Indianapolis IN "Functional Selectivity: a drug as both agonist and antagonist."

68. 1999-07-07. College of Veterinary Medicine, Mississippi State University. "Molecular aspects and consequences of ligand interaction with dopamine receptors."

69. 1999-09-13. NC Mental Health Meeting: Hargrave Award Address "Treatment of Psychiatric and Neurological Disorders: The Next Millenium", Southern Pines NC.

70. 1999-10-04. Department of Neuroscience, Columbia University. "Molecular recognition of dopamine D_1 receptors: towards novel therapeutics."

71. 1999-11-17. Neurology Grand Rounds, University of North Carolina, Chapel Hill. "Parkinson's disease: the neuroscience of therapeutic breakthroughs"

72. 2000-01-20. King's-Guy's-St. Thomas Schools of Medicine, London UK. "Novel D_1 Agonists in Parkinson's Pharmacotherapy"

73. 2000-04-06. Schering-Plough Pharmaceuticals, Kenilworth NJ. "Molecular mechanisms and therapeutic implications of dopamine D_1 agonists"

74. 2000-04-25. Memory Pharmaceuticals, New York, NY. "Mechanisms and application of novel dopamine agonists."

75. 2000-11-01. Parkinson Disease Center, Baylor University. "Novel pharmacotherapeutic approaches to the treatment of Parkinson's disease."

76. 2000-11-04. Society for Neuroscience, New Orleans, Annual Meeting. "The binding site of the dopamine D_1 and D_5 receptors" in Satellite Symposium "Subtype-selective molecular determinants of the 'binding-site crevice' of biogenic amine G protein-coupled receptors (GPCR)".

77. 2001-03-15. Pfizer, Inc., Groton CT. "Structural and functional studies of the activation of D_1 dopamine receptors and the implications for pharmacotherapeutics."

78. 2001-04-05. Emory University, Department of Neurology, Atlanta GA. "Structural and functional studies of the activation of D_1 dopamine receptors: implications for neurotherapeutics".

79. 2001-10-30. Biopsychology Program, University of North Carolina. "Biobehavioral Actions of Dopamine D_1 Agonists: From Computer to Clinic."

80. 2001-11-01. Case-Western University, Department of Biochemistry, Cleveland OH. "Structural and functional studies of the activation of D_1 dopamine receptors: implications for neurotherapeutics".

81. 2002-03-26. Parkinson's Disease Institute, Sunnyvale CA. "Parkinson's Disease Pharmacotherapy: The New from the Old."

82. 2002-04-05. University of North Carolina, Neuroscience Center. "The neuroscience of using drugs before Parkinson's disease is 'cured'."

83. 2002-06-12. NCDEU Annual Meeting, Boca Raton FL. "Current issues in the development of D_1 dopamine receptor agonists" in "New Approaches to the Treatment of Cognitive Disturbances in Schizophrenia."

84. 2002-09-09. Northwestern University, Division of Pulmonary and Critical Care Medicine. "Perspective on dopamine D_1 and mixed agonists: novel molecular mechanisms and therapeutic possibilities."

85. 2003-04-09. Lilly/Sphinx Pharmaceuticals. "Functional selectivity as a mechanism for novel drug discovery."

86. 2003-08-19. Pfizer Pharmaceuticals, Ann Arbor MI. "Functional selectivity and CNS drug action."

87. 2003-09-07. 14th Camerino-Noordwijkerhout Symposium "Ongoing Progress in the Receptor Chemistry," Camerino, Italy.

88. 2003-09-18. Purdue University Neuroscience Program. "Breakthrough Therapy for Parkinson's Disease: advances, however SLOW, SHAKE up old RIGID ideas."

89. 2003-12-11. American College of Neuropsychopharmacology Panel, San Juan. "Functional selectivity of dopamine receptor ligands predicts novel behavioral effects: examples from the lab (DAR-0101) to the clinic (aripiprazole)" in Panel "Functional Selectivity of Receptor Signaling: Epiphenomenon or New Opportunity for Drug Discovery?"

90. 2004-02-06. Columbia University, New York NY. "Functional selectivity of dopamine receptor ligands predicts novel behavioral effects."

91. 2005-04-02. EB2005 Meeting San Diego. [Panel Presentation]: "Functional selectivity of dopamine receptor ligands predicts novel behavioral effects."

92. 2005-04-05. EB2005 Meeting San Diego. [Panel Chair] "Are Pharmacology's Ten Commandments still viable? How functional selectivity affects teaching and research."

93. 2005-04-11. Psychiatric Drug Discovery & Development (SRI; Princeton NJ) "Full D_1 Agonists: Novel Treatment for Cognitive Deficits in Psychiatric Disorders."

94. 2005-06-02. Current Issues in the Development of D_1 Dopamine Receptor Agonists IN: D_1 Receptor Modulation and its Implications for Cognitive Enhancement in the Schizophrenia Spectrum. Annual Meeting of the Society of Biological Psychiatry, Atlanta. GA.

95. 2006-04-10. University of Michigan, Ann Arbor, Department of Pharmacology. Dopamine receptors and their ligands (the death of intrinsic efficacy!).

96. 2006-07-12. Cong. Int. Neuropsychopharmacol (CINP) Symposium. Does receptor functional selectivity contribute to atypicality? (Symposium). Chicago, Illinois.

ACADEMIC RESPONSIBILITIES AND SERVICE

ADMINISTRATIVE RESPONSIBILITES:

Founder & Faculty Director (1985-2002) of CSS, a 700 user multi-departmental IT Support group.

University Service: School of Medicine Conflict of Interest Committee (1998-2000); Vice Chancellor's Research Advisory Committee (1994-6); UNC Environmental Health Sciences Task Force (1993); Member of three medical school Chair or Director search committees.

Curriculum in Toxicology: Associate Director (2002-present); Executive Committee (elected: 1985-98); Admissions Committee (1985-8); Doctoral Written Exam Committee (1985-6; 1993-5).

Department of Pharmacology: [recent committees] Doctoral Exam Committee (2003-4; 1990-3); Graduate Education Executive Committee (1997-9); Admissions Committee (1985-8; 1993-6); Butler Awards Committee (1989-present); Graduate Program Review Committee (1994-7)

Neurobiology Curriculum: Faculty Membership Committee (1982-present)

TEACHING:

Teaching Awards:

Department of Pharmacology Teacher of the Year Award (1995): [voted by graduate students]

Current Teaching Responsibilities:

PHCO56: General Pharmacology. Course Coordinator plus 4 lecture hr.

NBIO722-3: Cellular and Molecular Neuroscience. 1996-present; "Receptor" block (half of 20 hr block) & 4 hr in Presynaptic mechanisms

PHCO202: Introduction to Pharmacology and Toxicology. CNS Coordinator plus 8 lecture hr.

PHCO123: Medical Pharmacology: Two lectures plus three workshops

BIO410: Introduction to Neurobiology. 1998-present; Lecture on dopamine and Parkinson's.

Tox222: Biochemical Toxicology. Receptor-Toxicant Interactions.

Past Teaching Responsibilities:

At UNC: 1997-9: **MS II: Medical Pharmacology**. CNS Coordinator plus 4 lecture hr. 1981-83; 1995-2004; **CBIO 117: The Cell:** Receptor theory and analysis (5 hr); **Dental Student Pharmacology**. CNS and Analgesic Pharmacology. 1981-1994; **Medical Problems II**. Preceptor. 1991-3; **Biotransformation of Xenobiotics.** Lectures on "Metabolism as determinant of action with CNS Drugs". 1982-1987; **Neurochemistry**. Section on "Receptors". 1982-present; **Synaptic Pharmacology**. Sections on "Neurotransmitters" and "Receptors". 1979-present; **BIOL 121: Introduction to Neurobiology**. "Dopamine Systems and Parkinson's disease." 1997-2000

At North Carolina State University: **Biochemical Toxicology**. Lectures on "Receptors" and "Neurotoxicology" (1973-1992); **Environmental Toxicology**. Three lectures per year on topical issues (1973-1987).

TRAINING:

Post-Doctoral trainees:

Mark H. Lewis, Ph.D.: 1980-3. Present/Last Known Position: Professor and Assoicate Chair, Univ. of Florida Health Sciences Center, Gainesville.

Diane L. DeHaven, Ph.D.: 1981-5. Present/Last Known Position: Director of Pharmacology, Adolar Pharma Inc.

Brian Kirkpatrick, M.D.: 1984-5. Current Position: Vice Chair and Professor, Department of Psychiatry, Medical College of Georgia.

Thomas Walsh, Ph.D.: 1985-6. Present/Last Known Position: Professor, Rutgers University (deceased, 2000).

Andrew Hoffman, Ph.D.: 1987-9. Present/Last Known Position: Computational Chemist, Polygen Inc.

Soon-Chul Lee, Ph.D.: 1989-90. Fogerty International Fellow. Professor, Chungnam University, Korea.

Parthena Martin, Ph.D.: 1987-89. Present/Last Known Position: Senior Scientist, Drug Discovery, PPD Development Inc.

Kirwin Darney, Ph.D.: 1989-1991. (No longer in science)

Cindy Lawler, Ph.D.: 1987-1991. Present/Last Known Position: Extramural Program Director, National Institute of Environmental Health Sciences, NIH.

John Petitto, M.D. 1990. (Research fellow 1988-9). Present/last known Position: Professor, University of Florida Health Sciences Center, Gainesville

John Gilmore, M.D.: 1990-1991. Present/Last Known Position: Professor of Psychiatry and Vice Chair for Research, University of North Carolina.

Larry Cook, Ph.D.: 1990-1991. Present/Last Known Position: Scientist, RTP, NC

Jeffrey Brock, Ph.D.: 1994-1996. Present/Last Known Position: Assistant Professor, Murray State University

Caryn Striplin, Ph.D.: 1995-1996. Present/Last Known Position: Research Scientist, Carolinas Medical Center, Charlotte.

Candace Andersson, Ph.D.: 1996-2000. Present position: Senior Medical Scientist, Bristol-Myers Squibb.

Bonita Blake, Ph.D.: 1996-1999. Present position: Assistant Professor, Center for Alcohol Studies, UNC

Mechelle M. Lewis, Ph.D.: 1997-2001. Present position: Research Fellow, Department of Neurology, UNC

Erin Heinzen, Ph.D., 2004-2005. Present position: Fellow, Duke University

Pre-Doctoral trainees:

Dan H. Mooney, Toxicology, M.S., 1993. Present/Last Known Position: Senior Toxicologist, Infineum USA L.P.

Peter O. Rau, Pharmacology, M.S., 1996. Present/Last Known Position: Clinical Research Scientist, Quintiles Inc.

Michael J. Twery, Ph.D., Pharmacology (co-chair), 1983. Present/Last Known Position: Staff Scientist, NHLBI

David Schulz, Ph.D., Neurobiology, 1985. Present/Last Known Position: Group Leader, Pfizer Inc.

Diane Niedzwiecki, Ph.D., Pharmacology, 1986. Present/Last Known Position: Toxicologist, State of Colorado

Vernon Jimmerson, Toxicology, Ph.D., 1989. Present/Last Known Position: Major, U.S. Army Chemical Defense Corps.

Beth Mileson, Toxicology, Ph.D., 1989. Present/Last Known Position: Associate Director, Toxicology, Ecotoxicology and Risk Assessment Division, Toxicology Sciences Group, Inc..

Timothy W. Lovenberg, Pharmacology, Ph.D., 1990. Present/Last Known Position: Group Leader, Johnson & Johnson Research Institute.

David Mottola, Pharmacology, Ph.D., 1992. Present/Last Known Position: United Therapeutics RTP, NC.

Val Watts, Pharmacology, Ph.D., 1994. Present/Last Known Position: Associate Professor of Medicinal Chemistry and Molecular Pharmacology, Purdue, University.

David Walker, Toxicology, Ph.D., 1995. Present/Last Known Position: Research Assistant Professor, Duke University Department of Pharmacology.
Hilary Smith, Neurobiology, Ph.D., M.D., 1996. Present/Last Known Position: Psychiatrist.
Mechelle Mayleben Lewis, Ph.D., Neurobiology, Ph.D., 1997. Present/Last Known position: Research Scientist, UNC.
Jason Kilts, Pharmacology, Ph.D. 1998. Present/Last Known position: Assistant Professor, Duke University.
Cassandra Prioleau, Pharmacology, Ph.D. 1998. Present/Last Known position: Scientist, US FDA
Diedra Montague, Pharmacology, Ph.D., 1999. Present position: Medical Sciences Representative, Bristol-Myers Squibb.
Elaine Arrington Gay, Neurobiology, Ph.D., 2003. Present Position: Postdoctoral fellow, NIH/NIEHS.
Amy Jassen, Neurobiology, Ph.D. 2003. Present position: Postdoctoral fellow, Harvard University.
Karen Neitzel, Neurobiology, Ph.D. 2004. Present position: Postdoctoral fellow, Emory University.
Jessica Ryman, Toxicology, Ph.D. 2004. Present position: Postdoctoral fellow, North Carolina State University.
Sarah Leonard, Pharmacology, Ph.D. 2004 Present position: Postdoctoral fellow, Wyeth Pharmaceuticals, Inc.
Scott Oloff, Pharmacology, Ph.D. 2005. Present Position: Research Scientist, Biogen, Inc.
Justin Corey Fowler, Medicinal Chemistry, Ph.D 2006. Present Position: Post-doc, Vanderbilt University.
Jonathan Urban, Toxicology, Ph.D. 2006. Present Position: Consulting Toxicologist, ChemRisk Inc..
Justin Brown, IBMS/Pharmacology (Ph.D expected 2007).

Honors Undergraduates:

Dalliah Black, UNC B.S., Biology, 1994. Present/Last Known position: M.D., Fellow in Surgery, UNC Hospitals.
J. Scott Overcash, UNC B.S., Biology, 1996. Present/Last Known position: M.D., UNC School of Medicine, 2000; Resident in Emergency Medicine, University of North Carolina Hospitals.
Clifford Peck, UNC B.S., Biology, 1996. Present/Last Known position: M.D., University of North Carolina School of Medicine, 2000.
Eric Volckmann, UNC B.S., Biology, 1998. Present/Last Known position: M.D., University of North Carolina School of Medicine, 2002
Subha Airan, UNC B.S., Biology, 2000. Present/Last Known position: MS IV, University of Maryland School of Medicine
Mehul Raval, UNC B.S., Biology, 2000. Present/Last Known position: MS IV, Wake Forest University School of Medicine
Olivia Granillo, UNC B.S., Biology, 2003. Current position: M.D./Ph.D. Student, Duke University
[Current: Meredith Gilliam, UNC B.S. Chemistry 2007; Michelle Oppenheim, UNC B.S. Chemistry 2007.]

EXHIBIT B

EXHIBIT B

- U.S. Patent No. 4,843,086
- U.S. Patent No. 4,886,812
- U.S. Application Serial No. 747,748
- EP Application 0 207 696
- BOE00075129-62